



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Grigori N. Enikolopov and John Mignone
Serial No.: 09/444,335 Group Art Unit: 1632
Filed: November 19, 1999 Examiner: Schnizer, R.
For: Transgenic Mice Expressing Fluorescent Protein in Multipotent Stem and Progenitor Cells

DEP & PEP
Room 307
#19 Reg-for Refund
08-06-01

CERTIFICATE OF MAILING		
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231		
on <u>7.17.01</u>	<u>Jenine Crump</u> Signature	
_____ <u>Jenine Crump</u> Typed or printed name of person signing certificate		

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US PATENT & TRADEMARK
OFFICE OF PAYMENT
REFUND UNIT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicant's Attorney received a Monthly Statement of Deposit Account, dated May 31, 2001, for Deposit Account No. 08-0380, indicating a charge of \$180.00 for submission of an Information Disclosure Statement (IDS) in the above-referenced application. The amount was charged to the Account on May 17, 2001. As explained below, the charge appears to be in error.

On May 16, 2001, a Second Supplemental IDS was hand delivered to the Examiner. The Second Supplemental IDS was submitted under 37 C.F.R. §1.97(c) together with the statement under 37 C.F.R. §1.97(e) that:

"Each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement"

The listed references were cited in an International Search Report (ISR) of the counterpart PCT application of the referenced application. Applicant's Attorney received the ISR on May 8, 2001 (copy of ISR enclosed). The ISR was included in the Second Supplemental IDS, along with the cited references.

Clearly, the references cited in the ISR were "first cited in ... a communication from a foreign patent office in a counterpart foreign application not more than three months prior to filing of" the Second Supplemental IDS.

Applicant's Attorney respectfully requests reimbursement of \$180.00 to Deposit Account No. 08-0380. A copy of this letter is enclosed for accounting purposes.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Anne J. Collins
Anne J. Collins
Registration No. 40,564
Telephone (781) 861-6240
Facsimile (781) 861-9540

Lexington, Massachusetts 02421-4799

Dated:

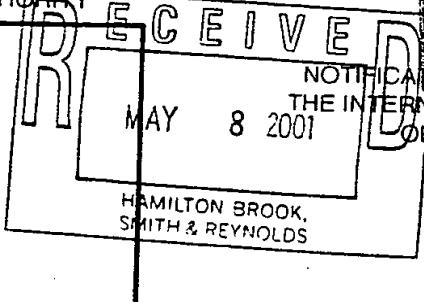
July 17, 2001



PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
HAMILTON, BROOK, SMITH &
REYNOLDS, P.C.
Attn. COLLINS, Anne J.
Two Militia Drive
Lexington, MA 02421
UNITED STATES OF AMERICA



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SEARCH DEPT.

NOTIFICATION OF TRANSMISSION OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year)

08/05/2001

Applicant's or agent's file reference 1314.1062002	FOR FURTHER ACTION	See paragraphs 1 and 4 below
International application No. PCT/US 00/ 31150	International filing date (day/month/year)	14/11/2000
Applicant COLD SPRING HARBOR LABORATORY et al.		

1. The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombelettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

08 JUN 2001 SPUR

[Signature]

2. The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

[Signature] Flewraffer

3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Authorized officer Chantal Meyer
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NOTES TO FORM PCT/ISA/220



These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

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OFFICE

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Office, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT



INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1314.1062002	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/31150	International filing date (day/month/year) 14/11/2000	(Earliest) Priority Date (day/month/year) 19/11/1999
Applicant COLD SPRING HARBOR LABORATORY et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

TRANSGENIC MICE EXPRESSING FLUORESCENT PROTEIN UNDER THE CONTROL OF THE NESTIN PROMOTER

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

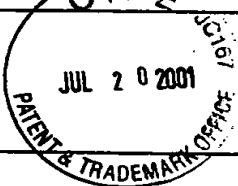
2

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/31150
O I P E

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/47 A01K67/027 C12N5/10



According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, WPI Data, PAJ, EPO-Internal, MEDLINE, SCISEARCH, EMBASE, BIOTECHNOLOGY ABS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	YAMAGUCHI MASAHIRO ET AL: "Visualization of neuronal stem cells in vivo." NEUROSCIENCE RESEARCH SUPPLEMENT, no. 22, 1998, page S286 XP000998227 21st Annual Meeting of the Japan Neuroscience Society and the First Joint Meeting of the Japan Neuroscience Society and the Japanese Society for Neurochemistry; Tokyo, Japan; September 21-23, 1998 ISSN: 0921-8696 abstract	1-5, 7, 9-13, 17, 20-22
Y	---	6-8, 14-16, 18, 19, 23-25, 28-30, 32, 34-49
	-/-	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

30 April 2001

Date of mailing of the international search report

08/05/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

ALCONADA RODRIG., A

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 00/31750

JUL 20 2001

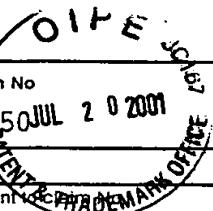
U.S. PATENT & TRADEMARK OFFICE

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WINKLER CHRISTIAN ET AL: "Incorporation and glial differentiation of mouse EGF-responsive neural progenitor cells after transplantation into the embryonic rat brain." MOLECULAR AND CELLULAR NEUROSCIENCE, vol. 11, no. 3, June 1998 (1998-06), pages 99-116, XP000998237 ISSN: 1044-7431 page 100, left-hand column, paragraph 3 -page 103, right-hand column, paragraph 1 ---	26, 27
Y	ROY NEETA SINGH ET AL: "Identification, isolation, and promoter-defined separation of mitotic oligodendrocyte progenitor cells from the adult human subcortical white matter." JOURNAL OF NEUROSCIENCE, vol. 19, no. 22, 15 November 1999 (1999-11-15), pages 9986-9995, XP000906926 ISSN: 0270-6474 figures 1, 2 ---	28-30, 32, 34-39
X	LOTHIAN CARINA ET AL: "An evolutionarily conserved region in the second intron of the human nestin gene directs gene expression to CNS progenitor cells and to early neural crest cells." EUROPEAN JOURNAL OF NEUROSCIENCE, vol. 9, no. 3, 1997, pages 452-462, XP000998218 ISSN: 0953-816X page 456, left-hand column, paragraph 2; figure 2 ---	20-22, 24
Y	ZIMMERMAN L ET AL: "Independent regulatory elements in the nestin gene direct transgene expression to neural stem cells or muscle precursors." NEURON, vol. 12, no. 1, January 1994 (1994-01), pages 11-24, XP000998222 page 21, paragraph 2; table 1 ---	6-8, 14-16, 18, 19, 23-25
Y	WO 99 19469 A (BIOTRANSPLANT INC) 22 April 1999 (1999-04-22) page 31, line 19 -page 34, line 17 ---	40-45
	-/-	

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/31150 JUL 20 2001



C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

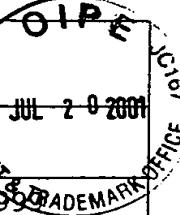
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim
Y	<p>REDDY ET AL: "Fluorescence activated sorting of totipotent embryonic stem cells expressing developmentally regulated lacZ fusion genes"</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, US, vol. 89, August 1992 (1992-08), pages 6721-6725, XP002115386 ISSN: 0027-8424 page 6724, left-hand column, paragraph 2</p> <p>-----</p>	40-45
Y	<p>DE 197 27 962 A (HESCHELER JUERGEN PROF DR UNIV) 14 January 1999 (1999-01-14) column 4, line 21-61; claim 13</p> <p>-----</p>	46-49

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/31150



Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9919469 A	22-04-1999	AU	1073899 A	03-05-1999
DE 19727962 A	14-01-1999	WO	9901552 A	14-01-1999
		EP	1002080 A	24-05-2000